REMARKS

Claims 1 and 3-4 were pending upon mailing of the present Office Action. Applicants have added new claims 22 and 23. Support for the amendment can be found throughout the specification as filed, for example, at Claim 11 (page 118) and pages 2-4. Accordingly, claims 1, 3-4 and 22-23 are currently under consideration in the Application. Reconsideration is respectfully requested in view of the following remarks.

Applicants wish to thank the Examiner for the productive telephone interview of January 4, 2006 during which the utility of the claimed polynucleotides was discussed with the undersigned agent and Dr. Barbara Zehentner. In particular, the Examiner indicated that the discussion materials (enclosed herein and discussed further below) forwarded to her by facsimile on January 3, 2006 were given to Michael Woodward for review and final decision. As discussed during the subsequent telephone conversation of January 11, 2006, the Examiner indicated that, following review of the application and the discussion materials, Michael Woodward concluded that the claimed polynucleotides satisfy the utility requirement. As such, it was agreed that Applicants would reply to the outstanding Final Office Action presenting the materials and arguments as discussed in the telephone interview of January 4, 2006. Also, Applicants requested consideration of additional composition claims. As per the telephone message of January 11, 2006, the Examiner indicated that it would be acceptable to include such claims.

Claim Rejections – 35 U.S.C. § 101 (Utility) and 35 U.S.C. § 112, first paragraph (enablement)

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 101 because the claimed invention allegedly lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility. The claims also stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement since one of skill in the art would not know how to make and use the claimed invention due to its alleged lack of utility. In particular, the Action contends that just because a polynucleotide is overexpressed in certain tissues is not an indication of the polynucleotide being of diagnostic value, if it had not been shown that a correlation between the overexpression and disease is

statistically significant. The Action notes that since only 30% of the cancer tissues show overexpression of the claimed sequence, then the claimed polynucleotide is not diagnostic of breast cancer. The Action further alleges that because the claimed polynucleotide is expressed in all normal breast tissue as well as breast tumor tissue, this contradicts the notion that the protein expressed from the claimed polynucleotide could be used for diagnostic purposes. The Action also contends that it is unclear how metastatic tumor cells can be detected using overexpression of SEQ ID NO:305 if this test detects only 30% of tissues with breast tumors and the sequence is expressed in 100% of normal breast tissue.

Applicants traverse the rejection on the following grounds. As an initial matter, and as noted during the interview of January 4, 2006, Applicants submit the following to clarify the data on the B854P antigen. In particular, as shown in Table 1 of the Declaration of Davin Dillon filed with Applicants' response filed July 26, 2004 (a copy is enclosed for convenience), the polynucleotide of SEQ ID NO:305 encodes a protein that is detected in 9 out of 10 breast cancer samples. This protein is also detected in 5 out of 5 normal breast samples (again, see Table 1). Real-time PCR shows that SEQ ID NO:305 is overexpressed in about 30% of breast tumors but is not detected in nearly all normal tissues. Note also that all metastatic breast cancer samples showed higher expression than that seen in normal breast. (see Figure 2 from Declaration of Dr. Dillon). Thus, the expression of the polynucleotide of SEQ ID NO:305 and the polypeptide it encodes is relatively breast tissue-specific and higher expression is observed in at least 30% of breast tumors as compared to expression in normal breast tissue and the majority of other normal tissues.

The expression pattern of B854P described above is nearly identical to that originally shown for mammaglobin, now a well-known breast cancer marker. See for example US Patent No. 5,668,267, issued based on the following data:

- Expression of mammaglobin was observed in normal breast tissue and breast cancer tissue, but not in a panel of other normal tissues. (See Figure 4B).
- Higher mammaglobin expression was observed in only about 27% of breast cancer samples tested. (see Figure 4A and Column 6, line 62).

The inventors conclude, "the expression of mammaglobin mRNA is relatively specific for mammary tissue" (see Column 13, line 15-16). Utility for detecting breast cancer was established based on this data and claims to the isolated polynucleotide issued on September 16, 1997.

Additionally, mammaglobin has been shown to be an effective marker for detecting breast cancer cells in peripheral blood: see Zehentner, *et al.* 2004 Clinical Chemistry 50:11 2069-2076. Using techniques described in the instant specification as filed (see for example at page 98, line 20-page 100, line 2), Zehentner, *et al.*, detect mammaglobin transcripts in circulating metastatic tumor cells in peripheral blood samples from breast cancer patients.

B854P antigen expression also has some similarity with the Her2/neu breast cancer antigen. The Her2/neu protein is overexpressed in **only 25-30% of breast cancers**. Furthermore, Her2/neu expression is not restricted to breast tissue but rather is found in most human cells. Yet, Her2/neu is useful for classification of breast cancers and its discovery led to the use of Herceptin™ for the treatment of those 25-30% of cancers that do express Her2/neu and to numerous FDA approved diagnostic kits for measuring the level of Her2/neu expression. See for example, enclosed article by M.S. Singer, Technology Spotlight.

Similar to mammaglobin, because the B854P sequence is expressed in breast tissue, but is not found in the majority of other normal tissues (in particular, normal resting and activated PBMC), one specific utility is the identification of breast-derived cells in secondary locations. For example, in patients diagnosed with breast cancer, identification of breast-derived cells in blood would indicate metastasis, a key piece of information for proper treatment regimen. In such a scenario, expression in colon would not bar utility of identification of breast-derived cells since the patient is already diagnosed as having breast cancer and it would be highly unlikely that the cells would be colon-derived. This type of utility has been confirmed by the skilled artisan as evidenced by the signed Declaration of Dr. Dillon filed with Applicants' response filed July 26, 2004.

In view of the above remarks, Applicants submit that the presently claimed polynucleotides are supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility. Accordingly, one of skill in the art would readily appreciate how to

make and use the claimed invention. Reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, is respectfully requested.

In view of the above amendments and remarks, the claims are now believed to be in condition for allowance. A good faith effort has been made to place the application in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at 206-622-4900 to resolve same.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

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JAU:mcs

Enclosures:

U.S. Patent No. 5,668,267
Zehentner, *et al.* 2004 Clinical Chemistry 50:11 2069-2076
Michael S. Singer, Technology Spotlight: Breast Cancer and HER-2/neu: Diagnostic Tools for Targeted Therapy
Copy of Declaration of Davin Dillon, originally filed with Applicants' response filed July 26, 2004.

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